Questions and Answers About the Study of Estrogen Replacement Therapy in Women Treated for Uterine Cancer

1. What is the Estrogen Replacement Therapy Study?

The Estrogen Replacement Therapy (ERT) Study is a clinical trial (research study) designed to resolve the debate over whether women who have had early stage cancer of the uterus, or endometrial cancer, can safely take ERT. It is one of many research studies sponsored by the National Cancer Institute (NCI) and carried out in medical centers around the country.

2. What is a clinical trial?

A clinical trial is a study with people that is designed to answer a question related to the diagnosis, treatment, prevention, or course of a disease. Such studies are designed to show how a particular approach—for instance, a promising treatment for a particular kind of cancer or a possible way to improve quality of life for cancer survivors—affects those who receive it. The study design is specified in a document called a protocol. Clinical trials are sometimes simply called protocols.

3. What is endometrial cancer?

Endometrial cancer is a form of cancer that originates in the endometrium (inner lining) of the uterus. Because most cancers of the uterus develop in this inner lining, the terms "cancer of the uterus" and "endometrial cancer" are often used interchangeably. Most women with endometrial cancer are treated with surgery to remove the uterus (hysterectomy) and bilateral salpingo-oophorectomy (removal of the ovaries and fallopian tubes).

4. What is ERT?

ERT is treatment often prescribed to reduce the discomforts of menopause, such as hot flashes, and to reduce the risk of osteoporosis (fragile bones) and heart disease in women after menopause.

5. Why is ERT after endometrial cancer controversial?

It has been commonly assumed that ERT is not safe for women with a history of endometrial cancer. Many physicians fear that ERT will increase a woman's chances of having the cancer reappear. (Even though the uterus has been removed, the cancer can recur in nearby tissues or spread to other parts of the body.)

There are several reasons for this assumption. One is that estrogen makes endometrial cancer cells grow in the laboratory. In addition, there is a good deal of evidence that estrogen, taken without progestins (another female hormone), can contribute to the *first* development of endometrial cancer.

However, two studies of patients with a history of endometrial cancer have suggested that ERT does not increase the risk of recurrence in selected patients. These findings have led to the current debate.

6. What is the evidence linking ERT with the first development of endometrial cancer?

Several large studies have found that women who take estrogen without progestins have a higher risk of developing endometrial cancer than women who do not use ERT. The risk for estrogen users is estimated to be 5 to 10 times higher than that for nonusers.

7. What is the evidence that ERT does not cause a recurrence of endometrial cancer?

Two studies have looked at data from groups of endometrial cancer survivors who used ERT. In one study, scientists analyzed data for 221 patients with stage I endometrial cancer, 47 of whom received estrogen for about 26 months after the tumor was removed. This study found that the cancer recurred in 15 percent of the women who did not receive estrogen and in 2 percent of those who did take estrogen.

In the other study, scientists analyzed data from 144 women who had stage I endometrial cancer, including 45 who were at low risk of recurrence and who had taken ERT for about 64 months. None of the estrogen users in this study had the cancer recur.

8. How will the new study be carried out?

More than 2,000 women who have had recent surgery for early stage uterine cancer (stage I or II) will take part in the study. Participants will be divided randomly (as in a flip of a coin) into two groups. One group will receive pills containing estrogen and the other will receive identical-appearing pills that do not contain estrogen (a placebo) for 3 years. The study is double-blinded—that is, neither physicians nor patients will know which women are taking the placebo and which are taking estrogen. Women in both groups will have check-ups every 6 months for 3 years and then annually for 2 more years.

9. Who is eligible for this study?

Women with endometrial cancer who were treated with a total hysterectomy and bilateral salpingo-oophorectomy and found to be at surgical stage IA, IB, IC, IIA, or IIB may be eligible for this study. These women must have at least one indication for ERT, including hot flashes, vaginal atrophy (dryness), increased risk of cardiovascular disease, or increased risk of osteoporosis. Women must have recovered from the effects of the recent surgery and be entered in the study within 12 weeks of surgery.

Women not eligible for this study include those with known or suspected breast cancer; those with a history of breast cancer, acute liver disease, or thromboembolic disease (blood clots); or those receiving other forms of hormonal therapy.

10. How can patients enroll in this study?

As in all NCI-sponsored clinical studies, patients are referred by a physician. Any health care provider can enroll patients in this study by contacting physicians who are members of NCI's Community Clinical Oncology Program (CCOP) or Cancer Therapy Evaluation Program (CTEP). For more information, health care providers may contact their nearest participating Gynecologic Oncology Group (GOG) or CCOP institution or call the GOG administrative office at 1–800–225–3053.

Patients may learn more about this study by calling the NCI's Cancer Information Service at 1–800–4–CANCER (see below).

11. How can people learn more about endometrial cancer?

The NCI's PDQ database has information for patients and physicians on diagnosing and treating endometrial cancer. In addition, a booklet for patients, called *What You Need To Know About™ Cancer of the Uterus*, is available from the NCI. Call 1–800–4–CANCER to ask for both the PDQ information and the booklet. PDQ is also accessible through the NCI Web site (see below).

Single, free copies of the pamphlets *Cancer of the Uterus* (APO97) or *Hormone Replacement Therapy* (APO66) are available from the American College of Obstetricians and Gynecologists (ACOG). For each pamphlet, send a stamped, self-addressed, business-size envelope along with the name of the pamphlet to ACOG, Resource Center, 409 12th Street, SW., Post Office Box 96920, Washington, DC 20090–6920. The ACOG Resource Center may also be reached by telephone at 202–863–2518, and requests may be faxed to 202–484–1595.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://www.cancer.gov to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@icicc.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 301–402–5874 and listen to recorded instructions.

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